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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,813	04/08/2004	Thomas A. Boyd	P0453.70112US01	9059

7590 12/27/2006

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EXAMINER	
GRAFFEO, MICHEL	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,813	BOYD ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 11, 14-32, 38-39, 41-46, 51-55, 56-70, 76-77, 80-88, 93, 95-96, 103-104 and 107-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 13 Dec 04 (1 sheet) 2 Feb 04 (1 sheet) 9 Aug 04 (3 sheets) 18 June 04 (6 sheets)
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-10,12,13,33-37,40,47-50,71-75,78,79,89-92,94,97-102,105 and 106.

DETAILED ACTION

Election/Restrictions

Applicant's election of methylnaltrexone and tegaserod maleate for oral administration in the reply filed on 31 July 2006 is acknowledged. To that end, claims 2-10, 12-13, 33-37, 40, 47-50, 71-75, 78-79, 89-92, 94, 97-102 and 105-106 are withdrawn from consideration there being no allowable linking claim. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Action

Claims 1, 11, 14-32, 38-39, 41-46, 51-55, 56-70, 76-77, 80-88, 93, 95-96, 103-104 and 107-114 are pending and examined.

Claim Objections

Claims 39, 77 and 96 are objected to because of the following informalities: the term "IM-indole" appears to be a misspelling. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 14, 21, 41-42, 45-46, 51-52, 60 and 80-84 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,176,186 to Goldberg et al.

Goldberg et al. teach a method for treating the intestinal mobility inhibiting (inducing laxation) side effects (see Abstract) of for example, methadone (see col 7 line 38) with quaternary derivatives of noroxymorphone (see Title and Abstract compound wherein R is cyclopropylmethyl) enterically or parenterally for example (see col 7 lines 48-56) via coated pills, tablets solutions, suspensions etc wherein the dosage unit is from 0.133mg/kg to 1.33mg/kg wherein calcium is not cited as a component.

Although Goldberg et al. do not specifically teach the plasma concentrations reached or time frame for treatment of the actives, such is necessarily the case since the dosage and administration is the same the plasma concentrations must be the same. Moreover, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical compound, the properties applicant discloses and/or claims are necessarily present.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 11, 14-32, 38-39, 41-46, 51-55, 56-70, 76-77, 80-88, 93, 95-96, 103-104 and 107-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,176,186 to Goldberg et al. in view of US Patent No. 5159081 to Cantrell et al. and further in view of US Patent No. 6986901 to Meisel et al.

Goldberg et al. teach a method for treating the intestinal mobility inhibiting (inducing laxation) side effects (see Abstract) of for example, methadone (see col 7 line 38) with quaternary derivatives of noroxymorpone (see Title and Abstract compound wherein R is cyclopropylmethyl) enterically or parenterally for example (see col 7 lines 48-56) via coated pills, tablets, solutions, suspensions etc wherein the dosage unit is from 0.133mg/kg to 1.33mg/kg wherein calcium is not cited as a component. Although

Goldberg et al. do not specifically teach the plasma concentrations reached or time frame for treatment of the actives, such is necessarily the case since the dosage and administration is the same the plasma concentrations must be the same. Moreover, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical compound, the properties applicant discloses and/or claims are necessarily present.

Goldberg et al. does not teach a method comprising tegaserod maleate wherein various symptoms are treated.

Cantrell et al. teaches that peripherally selective opioid antagonists are useful for the treatment of irritable bowel syndrome because the peripheral opioid peptides and their receptors have a major physiological role in the regulation of gut motility (see col 1 lines 10-20 and lines 55-64) and does not necessitate that a patient is undergoing exogenous opioid treatment. Cantrell et al. further show the use and efficacy of the compound on male mice (see col 57 line 32) and although no female patients are shown one of ordinary skill in the art would have found it obvious that a sample efficacious for males will also be efficacious for females or children. Although Cantrell et al. do not explicitly teach each and every symptom associated with irritable bowel syndrome, that the reference teaches the treatment of irritable bowel syndrome and constipation one of ordinary skill in the art would have found the symptoms associated therewith to be obvious in light of the teaching (i.e. that constipation and abdominal bloating/distension/pain are related).

Meisel et al. teach that tegaserod is efficacious in the treatment of irritable bowel disease (see col 6 line 49) and suggests that salts such as maleates are included in the invention and apply to essential ingredients (see col 3 lines 53-57) and when teaches the applicability of tegaserod, further mentions that the invention does not limit the essential ingredients to those listed (see col 6 line 49). Meisel et al. further teach that treatment for gastrointestinal issues includes sedatives and opiates (see col 1 lines 35-40) and antibiotics (see col 5 lines 35-40) which can be formulated for oral administration similarly to the teachings in Goldberg et al. wherein the compositions of the present invention may be formulated in sustained release form to provide the rate controlled release of any one or more of the components to optimize the therapeutic effects, i.e., analgesia, skeletal muscle relaxation, etc. while minimizing undesirable side effects. Suitable dosage forms for sustained release include layered tablets containing layers of varying disintegration rates or controlled release polymeric matrices impregnated with the active components and shaped in tablet form or capsules containing such impregnated or encapsulated porous polymeric matrices (see col 10 lines 66-end and col 11 lines 1-4). Although Meisel et al. do not explicitly recite a colonic site-directed formulation, the extensive and all inclusive nature of the teachings in Meisel et al. and Goldberg et al. as well suggest that the formulations recited are examples representative of a larger group of formulations i.e. any applicable formulation.

None of the references recite a kit comprising the above actives. Nonetheless, descriptive material that cannot exhibit any functional interrelationship with the way in

which computing processes are performed does not constitute a statutory process, machine, manufacture or composition of matter. Therefore, a package or kit would have been readily apparent one of ordinary skill in the art and such a package is obvious because absent factual evidence to the contrary, printed instruction on how to use is set forth in the combined references as is the combination and it would have been obvious to one of ordinary skill in the art that the combination of drugs would have been in a container which is, absent factual evidence to the contrary, the commercial package. Thus, the drug package and the instructions are obvious within the meaning of 35 U.S.C. 103. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

State of the Art

Yuan et al. Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: A double-blind randomized placebo-controlled trial. Clin. Pharmacol Ther. 1996;59:469-75 is considered an equivalent to US Patent No. 4,176,186 to Goldberg et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10 December 2006
MG

Ardin H. Marschel 12/10/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER